Complete Summary

GUIDELINE TITLE

Ethylene glycol exposure: an evidence-based consensus guideline for out-of hospital management.

BIBLIOGRAPHIC SOURCE(S)

Caravati EM, Erdman AR, Christianson G, Manoguerra AS, Booze LL, Woolf AD, Olson KR, Chyka PA, Scharman EJ, Wax PM, Keyes DC, Troutman WG. Ethylene glycol exposure: an evidence-based consensus guideline for out-of-hospital management. Clin Toxicol (Phila) 2005;43(5):327-45. PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Ethylene glycol poisoning

Note: This guideline applies to exposure of ethylene glycol alone. Exposure to additional substances could require different referral and management recommendation depending on the combined toxicities of the substances

GUIDELINE CATEGORY

Evaluation
Management
Risk Assessment

CLINICAL SPECIALTY

Emergency Medicine
Family Practice
Internal Medicine
Pediatrics

INTENDED USERS

Advanced Practice Nurses
Allied Health Personnel
Emergency Medical Technicians/Paramedics
Nurses
Physicians

GUIDELINE OBJECTIVE(S)

To assist U.S. poison center personnel in the appropriate out-of-hospital triage and initial management of patients with suspected exposure to ethylene glycol by

- Describing the process in which an exposure to ethylene glycol might be evaluated
- Identifying the key decision elements in managing cases of ethylene glycol exposure
- Providing clear and practical recommendations that reflect the current state of knowledge
- Identifying needs for research

TARGET POPULATION

Children, adolescents, and adults with acute and chronic ethylene glycol exposure

INTERVENTIONS AND PRACTICES CONSIDERED

Evaluation

1. Assessment of key decision points for triage:
    - Patient intent
    - Patient age and weight
    - Route of exposure and estimated dose of ethylene glycol
    - Time since exposure and symptoms

Management

1. Referral to an emergency department
2. Routine cleansing with mild soap and water for dermal exposures
3. Removal of contact lenses and immediate irrigation with room temperature tap water for ocular exposures, with referral for ophthalmologic exam, if symptoms of eye injury are present
4. Home observation

5. Gastrointestinal decontamination in the out-of-hospital setting with ipecac syrup, gastric lavage, or activated charcoal (considered but not recommended)
6. Administration of alcohol, fomepizole, thiamine, or pyridoxine (considered but not recommended in the out-of-hospital setting)

MAJOR OUTCOMES CONSIDERED

- Potentially toxic serum concentrations and potentially toxic dose of ethylene glycol in children, adolescents, and adults
- Onset of symptomatic toxic effects

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Literature Search

The National Library of Medicine's MEDLINE database was searched (1966 to September 2003) using ethylene glycol as a Medical Subject Heading (MeSH) term with the subheadings poisoning (po) or toxicity (to), limited to humans. The MEDLINE and PreMEDLINE (1966 to September 2003) were searched using ethylene glycol as textwords (title, abstract, MeSH term, CAS registry) plus poison* or overdos* or tox*, limited to humans. This same process was repeated in International Pharmaceutical Abstracts (1970 to September 2003, excluding abstracts of meeting presentations), Science Citation Index (1977 to September 2003), Database of Abstracts of Reviews of Effects (accessed September 2003), Cochrane Database of Systematic Reviews (accessed September 2003), and Cochrane Central Register of Controlled Trials (accessed September 2003). Reactions (1980 to September 2003), the ethylene glycol poisoning management in POISINDEX, and the bibliographies of recovered articles were reviewed to identify previously undiscovered articles. Furthermore, North American Congress of Clinical Toxicology abstracts published in the Journal of Toxicology-Clinical Toxicology (1995-2003) were reviewed for original human data. The chapter bibliographies in four major toxicology textbooks were reviewed for citations of additional articles with original human data. Finally, The Toxic Exposure Surveillance System (TESS) maintained by the American Association of Poison Control Centers was searched for deaths resulting from unintentional ethylene glycol poisoning or any deaths from ethylene glycol poisoning in children. These cases were abstracted for use by the panel.

Article Selection

The recovered citations were entered into an EndNote® library and duplicate entries were eliminated. The abstracts of these articles were reviewed, looking

specifically for those that dealt with estimations of exposure doses with or without subsequent signs or symptoms, time of onset of symptoms, and management techniques that might be suitable for out-of-hospital use (e.g., gastrointestinal decontamination). Articles were excluded that didn't meet the preceding criteria, didn't add new data (e.g., some reviews, editorials), or that exclusively described inpatient-only procedures (e.g., dialysis).

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Articles were assigned level-of-evidence scores based on the Grades of Recommendation table developed by the Centre for Evidence-Based Medicine at Oxford University. Single case reports were classified along with case series as level 4.

Levels of Evidence	Description of Study Design
1a	Systematic review (with homogeneity) of randomized clinical trials
1b	Individual randomized clinical trials (with narrow confidence interval)
1c	All or none (all patients died before the drug became available, but some now survive on it; or when some patients died before the drug became available, but none now die on it)
2a	Systematic review (with homogeneity) of cohort studies
2b	Individual cohort study (including low quality randomized clinical trial)
2c	"Outcomes" research
3a	Systemic review (with homogeneity) of case-control studies
3b	Individual case-control study
4	Case series, single case reports (and poor quality cohort and case control studies)
5	Expert opinion without explicit critical appraisal or based on physiology or bench research
6	Abstracts

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Data Extraction

All articles retrieved from the search were reviewed by a single abstractor. Each article was assigned a level of evidence score from 1 to 6 using the rating scheme developed by the Centre for Evidence-based Medicine at Oxford University (see the "Rating Scheme for the Strength of the Evidence" field); the complete paper was reviewed for original human data regarding the toxic effects of ethylene glycol or original human data directly relevant to the out-of-hospital management of patients with ethylene glycol toxicity or overdose. Relevant data (e.g., dose of ethylene glycol, resultant effects, time of onset of effects, therapeutic interventions or decontamination measures given, efficacy or results of any interventions, and overall patient outcome) were compiled into a table and a brief summary description of each article was written. This full evidence table is available at http://www.aapcc.org/DiscGuidelines/EGEvidenceTable.pdf.

The completed table of all abstracted articles was then forwarded to the panel members for review and consideration in developing the guideline. Every attempt was made to locate significant foreign language articles and have their crucial information extracted, translated, and tabulated. Copies of all of the abstracted articles were made available for reading by the panel members on a secure American Association of Poison Control Centers (AAPCC) website.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

An expert consensus panel was established to oversee the guideline development process (see Appendix 1 in the original guideline document). The American Association of Poison Control Centers (AAPCC), the American Academy of Clinical Toxicology (AACT), and the American College of Medical Toxicology (ACMT) appointed members of their organizations to serve as panel members. To serve on the expert consensus panel, an individual had to have an exceptional track record in clinical care and scientific research in toxicology, board certification as a clinical or medical toxicologist, significant U.S. poison center experience, and be an opinion leader with broad esteem. Two Specialists in Poison Information were included as full panel members to provide the viewpoint of the end-users of the guideline.

Guideline Writing and Review

A guideline draft was prepared by the primary author. The draft was submitted to the expert consensus panel for comment. Using a modified Delphi process, comments from the expert consensus panel members were collected, copied into a table of comments, and submitted to the primary author for response. The primary author responded to each comment in the table and, when appropriate, the guideline draft was modified to incorporate changes suggested by the panel. The revised guideline draft was again reviewed by the panel and, if there was no strong objection by any panelist to any of the changes made by the primary author, the draft was prepared for the external review process.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The rating scheme for the strength of the recommendation (A-D, Z) is directly tied to the level of evidence supporting the recommendation.

Grades of Recommendation	Levels of Evidence
A	1a
	1b
	1c
B	2a
	2b
	2c
	3a
	3b
C	4
D	5
Z	6

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

External review of the second draft was conducted by distributing it electronically to American Association of Poison Control Centers (AAPCC), American Academy of Clinical Toxicology (AACT), and American College of Medical Toxicology (ACMT) members and the secondary review panel. The secondary review panel consisted of representatives from the federal government, public health, emergency services, pediatrics, pharmacy practice, and consumer organizations (see Appendix 3 in the original guideline document). Comments were submitted via a discussion thread on the AAPCC web site or privately through email communication to AAPCC staff. All submitted comments were stripped of any information that would identify their sources, copied into a table of comments, and reviewed by the expert consensus panel and the primary author. The primary author responded to each comment in the table and his responses and subsequent changes in the guideline were reviewed and accepted by the panel. Following a meeting of the expert consensus panel, the final revision of the guideline was prepared.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Grades of recommendation (A-D, Z) and levels of evidence (1a-6) are defined at the end of the "Major Recommendations" field.

Note: Recommendations are in chronological order of likely clinical use. The grade of the recommendation is in parentheses.

1. Patients with exposure due to suspected self-harm, misuse, or potentially malicious administration should be referred to an emergency department immediately regardless of the doses reported (Grade D).
2. Patients with inhalation exposures will not develop systemic toxicity and can be managed out-of-hospital if asymptomatic (Grade B). Patients with clinically significant mucous membrane irritation should be referred for evaluation (Grade D).
3. Decontamination of dermal exposures should include routine cleansing with mild soap and water. Removal of contact lenses and immediate irrigation with room temperature tap water is recommended for ocular exposures. All patients with symptoms of eye injury should be referred for an ophthalmologic exam (Grade D).
4. Patients with symptoms of ethylene glycol poisoning (e.g., vomiting, slurred speech, ataxia, altered mental status) should be referred immediately for evaluation regardless of the reported doses (Grade C).
5. The absence of symptoms shortly after ingestion does not exclude a potentially toxic dose and should not be used as a triage criterion (Grade C).
6. Adults who ingest a "swallow" (10-30 mL), children who ingest more than a witnessed taste or lick, or if the amount is unknown of most ethylene glycol products should be referred immediately for evaluation. The potential toxic volume of very dilute solutions (e.g., product concentration known to be <20%) is larger and can be estimated by the formula (Formula 2) in the original guideline. If the concentration of the product is not known, it should be assumed to be a concentrated (>20%) product (Grade C).
7. A witnessed "taste or lick" only in a child, or an adult who unintentionally drinks and then expectorates all of a concentrated product without swallowing, does not need referral (Grade C).
8. Referral is not needed if it has been more than 24 hours since a potentially toxic unintentional exposure, the patient has been asymptomatic, and no alcohol was co-ingested (Grade D).
9. Gastrointestinal decontamination in the out-of-hospital setting with ipecac syrup, gastric lavage, or activated charcoal is not recommended. Transportation to an emergency department should not be delayed for any decontamination procedures (Grade D).
10. Patients meeting referral criteria should be evaluated at a hospital emergency department rather than a clinic. A facility that can quickly obtain an ethylene glycol serum concentration and has alcohol or fomepizole therapy available is preferred. This referral should be guided by local poison center procedures and community resources (Grade D).
11. The administration of alcohol, fomepizole, thiamine, or pyridoxine is not recommended in the out-of-hospital setting (Grade D).

Definitions:

Grades of Recommendation and Levels of Evidence

Grades of Recommendation	Levels of Evidence	Description of Study Design
A	1a	Systematic review (with homogeneity) of randomized clinical trials
	1b	Individual randomized clinical trials (with narrow confidence interval)
	1c	All or none (all patients died before the drug became available, but some now survive on it; or when some patients died before the drug became available, but none now die on it.)
B	2a	Systematic review (with homogeneity) of cohort studies
	2b	Individual cohort study (including low quality randomized clinical trial)
	2c	"Outcomes" research
	3a	Systemic review (with homogeneity) of case-control studies
	3b	Individual case-control study
C	4	Case series, single case reports (and poor quality cohort and case control studies)
D	5	Expert opinion without explicit critical appraisal or based on physiology or bench research
Z	6	Abstracts

CLINICAL ALGORITHM(S)

An algorithm is provided in Appendix 4 of the original guideline document for triage of patients with ethylene glycol ingestions.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations"). The strength of evidence for this guideline is limited to case series, case reports (level 4), one cohort inhalation study (level 2b) and one case-control study of ingestion (level 3b).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Appropriate out-of-hospital triage and initial management of patients with suspected ingestions of ethylene glycol
- Reduced unnecessary emergency department visits, reduced health care costs, optimized patient outcome, and reduced life disruption for patients and caregivers
- A more consistent approach to ethylene glycol exposure might facilitate research

POTENTIAL HARMS

Not stated

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

This guideline is based on an assessment of current scientific and clinical information. The panel recognizes that specific patient care decisions may be at variance with this guideline and are the prerogative of the patient and health professionals providing care, considering all of the circumstances involved.

Limitations of the Published Data

The strength of evidence for this guideline is limited to case series, case reports (level 4), one cohort inhalation study (level 2b) and one case-control study of ingestion (level 3b). Level 4 data do not provide a sound basis for toxic dose estimation or triage recommendations. The case reports and case series varied widely in the level of clinical detail presented, severity of clinical effects of the poisoning, timing of interventions, co-ingestants, estimated dose, and treatments administered.

The lack of precision in dose measurement is a major limitation of this literature analysis. The estimates are subject to many assumptions. Data for amount ingested are often inaccurate or incomplete. The history might be obtained from an intoxicated patient or an emotionally stressed friend or relative. Parents might under- or overestimate the ingested dose because of denial or anxiety. Poison center staffs often record the dose taken as the worst case scenario in order to provide a wide margin of safety. Estimating the volume ingested from examining most containers is unreliable. In most case reports and case series the estimates of exposure were not independently verified.

In most of the reports the exact time of ingestion was not reported or was not known. The time of onset of toxicity could only be estimated as occurring within a range of hours after the suspected ingestion in the majority of cases.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better

IOM DOMAIN

Effectiveness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Caravati EM, Erdman AR, Christianson G, Manoguerra AS, Booze LL, Woolf AD, Olson KR, Chyka PA, Scharman EJ, Wax PM, Keyes DC, Troutman WG. Ethylene glycol exposure: an evidence-based consensus guideline for out-of-hospital management. Clin Toxicol (Phila) 2005;43(5):327-45. PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2005 May 3

GUIDELINE DEVELOPER(S)

American Association of Poison Control Centers

SOURCE(S) OF FUNDING

Maternal and Child Health Bureau, Health Resources and Services Administration, U.S. Department of Health and Human Services

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

There are no potential conflicts of interest reported by the expert consensus panel or project staff regarding this guideline.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American Association of Poison Control Centers Web site.

Print copies: Available from the American Association of Poison Control Centers, 3201 New Mexico Avenue NW, Suite 330, Washington, DC 20016

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on October 28, 2005. The information was verified by the guideline developer on November 28, 2005.

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